Ventricular performance after onset of renal hypertension

C. M. FERRARIO, A. KOSOGLOV, R. BAJBUS AND G. R. NADZAM
Research Division, Cleveland Clinic Foundation, Cleveland, Ohio, U.S.A.

Summary

1. In renal hypertensive dogs, the slope of the relation between either stroke volume or cardiac output and end-diastolic pressure is shifted to the right of the normal curves.

2. The maximum to which stroke volume or cardiac output can be raised during loading is significantly less. These changes in cardiac performance appear to be unrelated to the severity of hypertension.

Key words: cardiac output, hypertension, left ventricular function.

Introduction

Previous experiments (Averill, Ferrario, Tarazi, Sen & Bajbus, 1976) have shown that long-term hypertension is accompanied by an unexpected decrease in both cardiac reserve and ventricular performance despite development of myocardial hypertrophy. The cause of this decrease in ventricular function is not known, nor do we know how soon these changes appear during the evolution of renal hypertension. The present series of experiments in dogs with and without renal hypertension was designed to clarify the latter point.

Methods

An electromagnetic flowmeter was placed around the ascending aorta and a Tygon catheter inserted into the left atrial appendage of sixteen healthy mongrel dogs. In six, both renal arteries were constricted 3 weeks after the implantation as described previously (Ferrario, Helmchen & McCubbin, 1975).

On the day of the experiment they were anaesthetized with chloralose (60 mg/kg, intravenously) after premedication with morphine (2 mg/kg, intramuscularly). A dual-tipped catheter pressure transducer was inserted into the aortic root via a brachial artery to record arterial and left ventricular pressures simultaneously. An additional larger catheter was passed into the right atrium via the right jugular vein for bleeding and infusion. The ECG was recorded from needle electrodes inserted into the limbs. Positive pressure respiration was used. After a 30 min control period, cardiac function curves were obtained by rapidly reducing and expanding the circulating blood volume with a roller pump connected to the large catheter inserted into the right atrium. Dogs were heparinized and bled to about 40% of their controlled cardiac output; the blood shed into the pump's reservoir was then returned into the animals along with 400 and 600 ml of Ringer's solution (36°C). Bleeding and infusion lasted approximately 2–3 min and repeated studies were spaced 20–30 min apart.

Analyses of pressure and flow signals, on a beat-by-beat basis, were performed with the aid of a digital computer. Ventricular function curves were obtained by plotting the beat-by-beat changes in stroke volume, cardiac output and stroke work as a function of either left ventricular end-diastolic or mean left atrial pressure as described previously (Averill et al., 1976). In addition, cardiac function curves are described mathematically according to the equation \( Y = A + Be^{-kx} \) as suggested by Bishop & Stone (1967).
Results

Left ventricular function curves obtained from the group of ten normal dogs were compared with those from hypertensive dogs 3 days after bilateral constriction of their renal arteries. Resting values differed in that hypertensive dogs had significant decreases in both stroke volume (range: 37-54%) and cardiac output. The latter fell to 1063 ± 24 (SEM) ml/min compared with 1520 ± 37 ml/min (P < 0.01) in the normal dogs. Cardiac rate increased in hypertensive dogs and left ventricular ejection rate fell significantly below normal values (0.163 ± 0.003 compared with 0.250 ± 0.002 s, P < 0.01). There were also differences among the hypertensive dogs in that arterial pressure was more severely elevated in two (147 ± 2 mmHg) than in the other four (110 ± 1 mmHg), and this difference was statistically significant (P < 0.01) when compared with each other and to the values obtained in normal dogs (90 ± 1 mmHg). Left ventricular end-diastolic pressure rose markedly in the two dogs with severe hypertension (12 ± 2 mmHg) but did not change in the four others (7 ± 3 mmHg); it averaged 9 ± 3 mmHg in the group of control dogs.

Fig. 1 shows the beat-by-beat changes in stroke volume as a function of left ventricular end-diastolic pressure for both the normal and renal hypertensive dogs. In contrast to normal dogs (Fig. 1a), the acutely hypertensive dogs showed a significant decrease in cardiac performance manifested by a sharp change in the ascending limb of the function curve and the maximum to which stroke volume could be raised during loading. This was also the case when cardiac output was plotted as a function of end-diastolic pressure. The decreased cardiac reserve was about the same regardless of the severity of hypertension and change in resting end-diastolic pressure.

The proportionality constant (K) of the one-compartment model for ventricular function was estimated for all three groups of dogs by the technique described by Bishop & Stone (1967). In dogs with mild hypertension, the value of K was below that of the normal dogs (0.137 mmHg⁻¹ compared with 0.178 mmHg⁻¹ respectively). This change may imply a decreased ventricular compliance, since small changes in stroke volume result in large changes in end-diastolic pressure. On the other hand, severe hypertension appears to result in a value of K greater than normal (K = 0.51 mmHg⁻¹). The resting output of these hypertensive dogs was practically equal to their maximum and fell precipitously with the slightest bleeding.

Discussion

The slope of the relation between stroke volume and left ventricular end-diastolic pressure and the maximum to which stroke volume can be raised by loading depicts the ability of the heart to perform as a pump. Under the circumstances of the present
Cardiac load in hypertension

experiments, dogs with renal hypertension of 3 days’ duration showed a decrease in cardiac performance unrelated to the arterial pressure. Ventricular function curves in acutely hypertensive dogs were displaced to the right of the normal curves, presumably due to an increase in left ventricular resting tension.

The observation that ventricular compliance, as interpreted by the alteration in $K$ values, differs among hypertensive dogs was totally unexpected and had not been reported previously. There is reason to believe that these changes are not related to afterload effects but this requires confirmation. Further, decreases in stroke volume both at rest and following stress are in accord with the decrease in stroke volume found in hypertensive patients in the absence of congestive failure. In view of what we know today, impaired cardiac pumping ability may be the cause of reduced minute output in patients with arterial hypertension.

In recent years, numerous investigators (see Guyton, Coleman, Bower & Granger, 1970, for review) have suggested that the heart may play a primary role in the pathogenesis of arterial hypertension, particularly in its early stages. On the contrary, our experiments concerning the mechanism for the rise in cardiac output early in hypertension suggested that it was related to a decrease in venous capacitance rather than a stage of increased myocardial contractility (Ferrario, Page & McCubbin, 1970). The present experiments appear to confirm this conclusion. A decrease in cardiac performance is present in both the acute and chronic phases of renal hypertension.

The nature of depressed ventricular function present in both acute and chronic renal hypertensive animals cannot be explained at present, but in accordance with previous observations (Averill et al., 1976) it may be related to changes in the structural composition of the myocardium induced by the renal pressor system.

References


